HOUSE OF COMMONS SESSION 1997–98

SCIENCE AND TECHNOLOGY COMMITTEE

Fifth Report

BRITISH BIOTECH

Volume I

Report and Proceedings of the Committee

Ordered by The House of Commons *to be printed*
13 August 1998
pursuant to Standing Order No. 137

LONDON: THE STATIONERY OFFICE
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The Science and Technology Committee is appointed under Standing Order No. 152 to examine the expenditure, administration and policy of the Office of Science and Technology and associated public bodies.

The Committee consists of 11 Members. It has a quorum of three. Unless the House otherwise orders, all Members nominated to the Committee continue to be Members of it for the remainder of the Parliament.

The Committee has power:

(a) to send for persons, papers and records, to sit notwithstanding any adjournment of the House, to adjourn from place to place, and to report from time to time;

(b) to appoint specialist advisers either to supply information which is not readily available or to elucidate matters of complexity within the Committee's order of reference;

(c) to communicate to any other such committee and to the Committee of Public Accounts, the Deregulation Committee and the Environmental Audit Committee its evidence and any other documents relating to matters of common interest; and

(d) to meet concurrently with any other such committee for the purposes of deliberating, taking evidence, or considering draft reports.

The following were nominated Members of the Committee on 14 July 1997:

Mr David Atkinson
Mr Nigel Beard
Dr Michael Clark
Mrs Claire Curtis-Thomas
Dr Ian Gibson
Dr Lynne Jones
Mr Nigel Jones
Dr Ashok Kumar
Mrs Caroline Spelman
Dr Desmond Turner
Dr Alan W Williams

Dr Michael Clark was elected Chairman on 30 July 1997.

On 22 June 1998 Mrs Caroline Spelman was discharged from and Mrs Jacqui Lait added to the Committee.

The cost of printing and publishing this Report is estimated by The Stationery Office Limited at £590.

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2. **Dr Millar's actions in briefing Perpetual, while certainly unusual, seem more the product of difficulties at British Biotech than the origin of them (paragraph 9).**

3. **In an environment where subjective judgements and sentiment are so important in determining share price and company value, and where investors are to a large degree dependent upon the company to inform those judgements, "the accuracy, precision and objectivity of information released ... is vital" (paragraph 12).**

4. **We recommend that the Government, through the regulatory system, encourage all biotechnology companies to make full use of external scientific expertise and advice (paragraph 13).**

5. **We recommend that the Medicines Control Agency and the European Agency for the Evaluation of Medicinal Products work with the Stock Exchange to resolve any potential conflicts between their respective regulatory regimes affecting the biotechnology sector (paragraph 14).**

6. **Biotechnology companies should be able to call on appropriate expertise for all areas of company activity and strive to reach a balance among their non-executive directors between those who can offer crucial business development expertise and those who are familiar with the risks and vicissitudes of drug development (paragraph 15).**

7. **It is too early to determine precisely what, if any, will be the long-term impact on investor confidence and future investment in the biotechnology sector (paragraph 16).**

FIFTH REPORT

The Science and Technology Committee has agreed to the following Report:—

BRITISH BIOTECH

Introduction

1. British Biotech plc was established in 1986 with the aim of combining approaches in molecular biology and synthetic chemistry to develop new therapies for the treatment of cancer. It has also pursued research into inflammatory, vascular and viral diseases including AIDS. In 1992 it became the first UK biotechnology company to be publicly listed; the initial flotation share price of 42.5 pence rose to a high of around £3.70 in May 1996, with market capitalisation reaching nearly £2 billion.[1] It has been widely seen as the "flagship of the UK biotechnology sector".[2]

2. On 11th March 1998 British Biotech suspended its Head of Clinical Research, Dr Andrew Millar, pending an investigation into breaches of company policy. Rumours of Dr Millar's suspension that day and their confirmation by British Biotech the following day caused the company's share price to drop by 15.5 pence to 70 pence.[3] Media interest was keen and became intense as it emerged that Dr Millar had raised questions about the company's corporate strategy.[4] When, on 20th April 1998, British Biotech announced that Dr Millar had been dismissed for discussing confidential company information with third parties it also stated that, following investigations, "the Board is satisfied that these matters [raised by Dr Millar] either had no substance or reflected purely personal opinions held by Dr Millar".[5] British Biotech's shares fell further and media interest persisted. On 28th April 1998 Dr Millar sent an open letter to *The Financial Times* which confirmed what had already been widely trailed in the press; namely that he believed that the results of on-going clinical trials were unlikely to lead to licensable or marketable drugs within the time-frame envisaged by the company.[6] His concerns extended to the management of clinical trials, the accuracy of information released by the company to the press, and share dealings on the part of the directors.

3. Given our remit over science and technology, we maintain an active interest in the UK biotechnology industry, both as an example of a genuinely innovative and innovating industry firmly rooted in the UK science base and in terms of its potential to create wealth and improve quality of life for UK citizens. Consequently we watched with concern the events at British Biotech and the associated media coverage, fearing that they could have a profound and detrimental effect on the reputation of the entire UK biotechnology industry and thus on its ability to continue to attract investment and develop innovative and useful products. As the London Stock Exchange told us "adverse publicity for a leading participant in any industry may have an impact on the sector as a whole. This is particularly so for sectors which rely heavily on investor confidence in long term research and development programmes".[7] It was for these reasons that on the day on which Dr Millar's open letter to *The Financial Times* was published we decided to conduct this inquiry. **It is not our role to pass judgement on alleged misdemeanours nor to assess the propriety of personal share dealings and we make no attempt to do so.**

4. During the course of the inquiry we have solicited written evidence from many of those involved with British Biotech, receiving 21 memoranda in total. We have also taken oral evidence from: Drs Keith McCullagh and Peder Jensen, respectively Chief Executive and Director of Development at British Biotech; Dr Andrew Millar, former Head of Clinical Research, British Biotech; Ms Jane Henderson, a market analyst at Goldman Sachs; Dresdner

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[1] Average share prices in the biotechnology sector fell by some 40% during 1997. By the end of 1997 British Biotech shares stood at around £1.
[2] Eg *Financial Times*, 21 May 1998.
[3] HC 888-ii (Session 1997-98) (Memorandum from Perpetual Investment Management Services, Annex).
[4] Eg *The Times*, 16 March 1998.
[5] British Biotech News Release, 20 April 1998
[6] HC 888-i (Session 1997-98) (Memorandum from Dr Millar, Annex). *The Financial Times* published an edited version of this letter on 29th April 1998.
[7] HC 888-II (Session 1997-98), Appendix 3, para 4.4.

Kleinwort Benson — advisers, bankers and brokers to British Biotech; Perpetual Investment Management Services, British Biotech's second largest shareholder; and Dr Peter Lewis, Director of Research and Development at British Biotech from 1992 until May 1997. We extend our thanks to our specialist adviser for this inquiry, Professor Derek Burke, former Vice-Chancellor of the University of East Anglia.

British Biotech

5. Most biotechnology companies seek to discover a molecule with potential to be developed as a pharmaceutical treatment for a particular illness or disorder. Once a potentially useful molecule has been discovered, substantial development is required to establish efficacy, safety and optimum delivery methods before the drug can be commercialised or gain regulatory approval. The development phase is risky, with no guarantee that a particular product will ever come to market, and, compared to research, is very expensive. Consequently many companies have opted to mitigate the risks by selling their discovery to, or entering a joint partnership with, an established pharmaceutical company capable of funding the development and providing the requisite scientific skills. British Biotech told us that some biotechnology companies had commercialised their own products, particularly in home markets, but no examples were given.[8] British Biotech decided on the high-risk, and potentially high-return, strategy of taking its cancer drugs, particularly Marimastat, to market in the US and Europe alone while partnering a Japanese company to bring the drugs to market there and it raised capital through its 1996 rights issue on that basis.[9]

6. It is clear that there had been differences within the Board of Directors from 1995 onwards — four executive directors left the company — and, in addition, there were particular differences between Drs McCullagh and Millar, the latter of whom was not a main board director. In 1995 they disagreed over whether phase III clinical trials on Batimastat, an injectable anti-cancer drug, should be halted and, once they had, over whether they should be re-started; over the tone of the press release announcing that the trials had been halted, which Dr Millar believes portrayed an over-optimistic picture;[10] over the tone and content of press releases regarding the progress of clinical trials of Marimastat, an orally delivered anti-cancer treatment; and over British Biotech's potential pancreatitis treatment, Zacutex. There were also apparent differences from time to time over the designation and nature of, and the interpretation of data from, clinical trials.[11] The net result of Dr Millar's more pessimistic interpretation of the data from clinical trials, and his perhaps more cautious attitude to corporate strategy, led him to the conclusion that "the Board were running a business plan consistent only with extreme and unfounded optimism".[12] Dr Millar summarised his concerns by telling us that "my view is that a business `charade' had been built up and was preventing acknowledgement of data which differed from previous overpromises. This in turn, perverted the decision making process so that projects were no longer managed in their best long term interests. In effect the business charade had become bigger than the science".[13]

7. In January 1995 when, according to Dr Millar, the future of the Batimastat trials was already in question, several British Biotech board directors sold a substantial number of shares in the company a month in advance of the public announcement that the Batimastat trials had been halted. The propriety of share dealing is a matter not for us but for the London Stock Exchange. It investigated these share dealings in 1995 to see if they contravened the code of practice governing directors' share dealings. At that time the Stock Exchange concluded "that there was no basis for disciplinary action",[14] but it has recently re-opened its investigation in response to Dr Millar's disclosure of information and allegations.

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[8] HC 888–i (Session 1997-98) (Supplementary Memorandum from British Biotech, para B3).
[9] Q. 104.
[10] HC 888–i (Session 1997–98) (Affidavit from Dr Millar, paras 25–27); Q. 58; British Biotech, *Circular to Shareholders*, pp20-22.
[11] HC 888–i (Session 1997–98) (Affidavit from Dr Millar, paras 32 and 60).
[12] HC 888–i (Session 1997–98) (Memorandum from Dr Millar, Annex).
[13] HC 888–i (Session 1997–98) (Memorandum from Dr Millar, para 2).
[14] HC 888–II (Session 1997–98) Appendix 3, para 3.5

8. Dr Millar's concerns may have been, in part and for a limited time, based on information that was not available to others. In the period from November 1996 to April 1997 Dr Millar "unblinded" data from the on-going clinical trials on Marimastat and Zacutex.[15] Dr Millar claims that he verbally informed Dr Lewis, his immediate line manager, that he was performing analysis on unblinded data at the time, in the full expectation that his pessimistic findings would be passed on to the Chief Executive, Dr McCullagh.[16] Dr Lewis denies this.[17] Dr Millar's unblinding of clinical trials was made known to Dr McCullagh in May 1997 when Dr Millar informed him personally.[18] The unblinding of clinical trials is ethically questionable: although permissible in certain circumstances and desirable if patient safety is thought to be at risk, a determination of whether justified in any particular circumstances is a matter for experts. It is for the drug regulatory bodies — the Medicines Control Agency in the UK, the European Agency for the Evaluation of Medicinal Products in Europe and the Food and Drug Administration in the US — to determine whether unblinded trials have been invalidated for regulatory purposes.

9. Dr Millar was not the only member of staff at British Biotech to question corporate strategy. Dr Lewis, for instance, told us he had "a series of disagreements with the Chief Executive ... about his strategy for the company" and that "Dr McCullagh had hugely ambitious plans".[19] Dr Lewis' reaction to the failure of his attempts to moderate corporate strategy was to offer his resignation in January 1997. Dr Millar's was to take an opportunity offered to inform British Biotech's second largest shareholders, Perpetual Investment Management Services, about his concerns, which he did on 18th February 1998. **Dr Millar's actions in briefing Perpetual, while certainly unusual, seem more the product of difficulties at British Biotech than the origin of them.**

10. Dr Millar makes serious allegations concerning share dealing, news management and corporate strategy. We welcome the investigations which are currently underway at the Stock Exchange and commend the evidence we have received to it.

Implications for the Biotechnology Industry

11. There are clearly inherent difficulties for small drug discovery companies in conducting the full series of pre-clinical and clinical trials which is necessary before a drug can be brought to market without the financial and scientific backing of a larger partner. Creating a new fully integrated pharmaceutical company is an ambitious objective with high risks and potentially high rewards. Decisions on whether to support such a strategy must be taken by directors and investors alike, cognisant of the risks involved.

12. Share prices in biotechnology companies are very volatile. Most biotechnology companies have no assets other than the cash which they have raised from investors and, at the outset, have no products to sell. Thus decisions on whether or not to invest must be based on judgements about the potential of scientific intellectual property and scientific expertise and the capability of the company's management to turn such scientific assets into useful and marketable products. Furthermore, as Perpetual pointed out "diseases like Cancer, Alzheimer's and AIDS, give rise to strong emotions" which serve to increase market speculation.[20] Investment in the biotechnology sector is therefore high risk and consequently, as Mercury Asset Management told us, "The investment community attaches a risk premium to such ventures [and] this level of the risk premium inevitably fluctuates with events".[21] This volatility, together with the dependence

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[15] Many clinical trials involve comparing the effects of drugs under development against an existing treatment and a placebo. In double-blinded studies, neither patients nor anyone else involved in the trial is aware of which of the three possible treatments a particular patient is receiving thus ensuring that researchers and others involved in the trials cannot be influenced in their trial management or data assessment and therefore cannot bias results.

[16] HC 888–i (Session 1997–98) (Memorandum from Dr Millar, Annex).

[17] QQ. 389-90.

[18] Q. 55.

[19] HC 888–iii (Session 1997–98) (Memorandum from Dr Lewis). *See also* HC 888–II, Appendix 5.

[20] HC 888–ii (Session 1997–98) (Memorandum from Perpetual Investment Management Services, para 4.5). The *New York Times* recently carried a front page story about a product which suggested that it was successful in reducing the blood supply to cancer tumours in mice, thus shrinking the tumours. The company's share price rose dramatically but it cautioned investors about over optimism on a product that, at best, would not reach the market for many years. Over the week the company's shares rose from $12 to over $80 and then fell back to $33.

[21] HC 888–II (Session 1997–98), Appendix 4, para 16.

of the company on success in clinical trials, could put scientific objectivity at risk if researchers are put under pressure to produce or interpret results in a manner which will maintain investor confidence and share prices. Thus, **in an environment where subjective judgements and sentiment are so important in determining share price and company value, and where investors are to a large degree dependent upon the company to inform those judgements, "the accuracy, precision and objectivity of information released ... is vital".**[22]

13. We were surprised to learn that not all biotechnology companies in the UK make use of an external scientific advisory board to validate clinical trials.[23] Such a device could serve not only as a source of valuable scientific expertise but also as a means of protecting scientific objectivity. **We recommend that the Government, through the regulatory system, encourage all biotechnology companies to make full use of external scientific expertise and advice.**

14. During the course of our inquiry concerns have also been raised about a possible conflict between the needs of investors for regular progress reports on drug development and the regulatory prohibitions against promotion of drugs before they are licensed.[24] British Biotech told us "in meeting the requirements of the regulatory agencies, a biotech company can frequently face conflict with the financial requirements for news flow and information".[25] Dresdner Kleinwort Benson, while unconvinced that there was a conflict, in the strict sense, accepted that appropriate news management was "certainly a problem for biotech companies".[26] **We recommend that the Medicines Control Agency and the European Agency for the Evaluation of Medicinal Products work with the Stock Exchange to resolve any potential conflicts between their respective regulatory regimes affecting the biotechnology sector.**

15. When hi-tech companies are first launched it is often with the assistance of venture capitalists who place specialists on the board as non-executive directors. Once the company has become public, these specialists are gradually replaced with the company's own appointees. Several witnesses to our inquiry stressed the importance of ensuring that there were, among the non-executives directors of biotechnology companies, sufficient people who had direct experience of drug development.[27] From the evidence before us we have no grounds to make any criticism of individual non-executive directors at British Biotech but it seems obvious to us that **biotechnology companies should be able to call on appropriate expertise for all areas of company activity and strive to reach a balance among their non-executive directors between those who can offer crucial business development expertise and those who are familiar with the risks and vicissitudes of drug development**. This does not seem to have been the case at British Biotech when the board was altered after flotation and probably contributed to its problems.

16. Witnesses were divided in their opinions over whether our initial fears that the British Biotech saga would serve to undermine investor confidence in the entire biotechnology sector were well founded. Although so far this year the biotechnology sector's performance has been below the average for the stock market as a whole,[28] it is difficult to attribute the cause of general market movements to any particular events and, as Dresdner Kleinwort Benson pointed out, "over the last year or so, many companies in the sector, as well as British Biotech, have had to announce events which have adversely affected market perception, such as the failure of lead compounds and the replacement of chief executives".[29] As the London Stock Exchange agreed, **it is too early to determine precisely what, if any, will be the long-term impact on investor confidence and future investment in the biotechnology sector.**[30]

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[22] HC 888–ii (Session 1997–98) (Memorandum from Perpetual Investment Management Services, para 4.5).
[23] HC 888–II (Session 1997–98), Appendix 5.
[24] Eg HC 888–i (Session 1997–98) (Supplementary Memorandum from British Biotech, para A1).
[25] HC 888–i (Session 1997–98) (Supplementary Memorandum from British Biotech, para B8).
[26] HC 888–ii (Session 1997–98) (Memorandum from Dresdner Kleinwort Benson).
[27] Eg Q. 496; HC 888–II (Session 1997–98), Appendix 5.
[28] HC 888–II (Session 1997–98), Appendix 3, para 4.5.
[29] HC 888–ii (Session 1997–98) (Memorandum from Dresdner Kleinwort Benson).
[30] HC 888–II (Session 1997–98) Appendix 3, para 4.5.

17. The biotechnology industry, as a leading research based industry, will always be of interest to us. We will follow the fortunes of British Biotech, under the leadership of a new Chairman and a new Chief Executive, and shall continue to report on issues affecting the biotechnology sector as appropriate.

PROCEEDINGS OF THE COMMITTEE RELATING TO THE REPORT

Thursday 13th August 1998

Members present:

Dr Ian Gibson
Dr Ashok Kumar
Mrs Jacqui Lait
Dr Desmond Turner
Dr Alan W. Williams

In the absence of the Chairman, Dr Alan W. Williams was called to the Chair.

The Committee deliberated.

* * *

Draft Report (British Biotech), proposed by Dr Alan W. Williams, brought up and read.

Ordered, That the draft Report be read a second time, paragraph by paragraph.

Paragraphs 1 to 17 read and agreed to.

Resolved, That the Report be the Fifth Report of the Committee to the House.

Ordered, That Dr Alan W. Williams do make the Report to the House.

Ordered, That the provisions of Standing Order No. 134 (Select committees (reports)) be applied to the Report.

Several Papers were ordered to be appended to the Minutes of Evidence.

Several Memoranda were reported to the House.

The Committee deliberated.

* * *

[Adjourned till Wednesday 21st October
at a quarter to Four o'clock

LIST OF WITNESSES

Wednesday 1 July 1998

BRITISH BIOTECH PLC
Dr Keith McCullagh and Dr Peder Jensen

DR ANDREW MILLAR
former Head of Clinical Research, British Biotech

Wednesday 15 July 1998

MS JANE HENDERSON
Goldman Sachs

PERPETUAL INVESTMENT MANAGEMENT SERVICES
Mr Bob Yerbury, Mr Neil Woodford and Mrs Margaret Roddan

DRESDNER KLEINWORT BENSON
Mr T G Barker, Mr Peter Button and Mr Simon Neathercoat

Tuesday 28 July 1998

DR PETER LEWIS
former Director of Research and Development, British Biotech

LIST OF MEMORANDA INCLUDED IN THE MINUTES OF EVIDENCE

LIST OF APPENDICES TO THE MINUTES OF EVIDENCE

Volume II

MEMORANDA REPORTED TO THE HOUSE BUT NOT PRINTED

1. Memoranda from HSBC Securities
2. Memorandum from British Biotech plc

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